REMARKS

Claims 1-3, 5, 7-9, 13-22, 24-31, and 33-38 are pending. Claims 4, 6, 10-12, and 23 have been canceled without prejudice or disclaimer to the subject matter contained therein. Claims 1, 7, 13, 15, 18-19, and 31 have been amended to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Support for the amendment to Claim 1 can be found on page 4, line 25 to page 5, line 7, as well as page 7, lines 6-11, page 8, lines 1-5, and page 12, lines 13-17. Support for the amendment to Claim 7 can be found on page 7, lines 4-11, page 11, lines 20-23, and page 15, lines 6-9. Support for the amendment to Claim 13 can be found on page 12, lines 9-11. Claim 15 was amended to refer to a non-canceled claim. Support for the amendment to Claim 18 can be found on page 8, lines 1-5. New Claims 37 and 38 have been added. Support for new Claim 37 can be found on page 17, line 10 through page 18, line 12 and Figures 3-5. Support for new Claim 38 can be found on page 17, lines 14-16 and Figure 3-5. No new matter is added by way of the amended or new claims. The amendments are believed to place the claims in better condition for allowance and the new claims are believed to be allowable.

REJECTIONS

Rejection of Claims 1-18 under 35 USC § 112, second paragraph

The Examiner has rejected claims 1-18 under 35 U.S.C. § 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner states:

> The phrase "sample components to be harvested from said sample" in Claim 1 lines 4-5 is vague and indefinite because it is unclear as to the basis for this limitation in the claim method
>
> of separating components from a sample.

Applicants respectively traverse this rejection, but have amended the claim to advance prosecution.

Claim 1 has been amended to clarify that the sample is separated into components. Withdrawal and reconsideration of the rejection is respectfully requested.

Rejection of Claims 1, 5-7, 13, and 15-17 35 USC § 102 (b) over Levine et al. (5,635,362)

The Examiner has rejected claims 1, 5-7, 13, and 15-17 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 5,635,362 to Levine et al. (Levine '362). The Examiner alleges the method of Levine '362 teaches the device and method for the analysis of a blood sample for the presence or absence of one or more target analytes that are caused to settle in a predetermined location in a transparent tube (col. 1, line 9-18). Applicants respectfully traverse this rejection.

The present invention discloses and claims a method for separating components in a sample. The method entails mixing the sample of interest with particulate carriers having antibodies bound thereto that have an affinity for the target in a container that has a focusing device with a passage for receiving and elongating layers of the sample and centrifuging the container and sample to separate the components of the sample by forcing the target component into the passage.

Levine '362 does not teach a float that contains a passage that receives and elongates the layers of the sample. The present claimed invention has a focusing device with a passage for receiving and elongating layers of the sample. Further, the target components are forced into the passage. In Levine '362, the sample is forced between the insert and the container wall. (See col. 3, lines 1-5); however, this is not a passage of the focusing device. As Levine '362 does not contain every element of the claimed invention, it does not anticipate the claimed invention. Withdrawal and reconsideration of the rejection is respectfully requested.

Rejection of Claims 1-7, 13, and 15-17 under 35 USC § 103 (a) over Levine et al. (U.S. 5,635,362) and Levine et al. (5,393,674)

The Examiner has rejected claims 1-7, 13, and 15-17 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,635,362 (Levine '362) to Levine et al. in view of U.S. Patent 5,393,674 to Levine et al. (Levine '674). The Examiner states Levine '362 differs from the instant invention in failing to include in the method step of removing the target component, and that the float includes ribs. The Examiner further states Levine'674 teaches a float formed with a core portion that has a through bore (channel), and an annular sleeve portion (ribs). The Examiner concludes:

> It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Levine #1 ['362] by incorporating the method step of removing the target component as taught by Levine #2 ['674] because it would provide the advantage of performing multiple methods such as cell concentration, assay, and harvesting in a unitary sealed tube (Levine #2: col 1, lines 41-57). This would also reduce exposure of contaminated blood to the technician and the disposal of contaminated blood would be in a stable, inert environment. The ribs of the float would provide a ten fold expansion of the white cell and platelet layers when performing the cell harvesting with the tube-float combination (Levine #2 col. 2, lines 50-60). Therefore, one would have had reasonable expectation of success of incorporating the method step of removing the target component into the

> method of Levine #1 because both Levine #1 and Levine #2 teaches the method of cell separation.

Applicants respectively traverse this rejection but have amended the claim to advance prosecution.

Claim 1 has been amended to include the particulate carriers having a specific density and size. Levine '362 teaches a one-step method for determining the presence or absence of a target analyte in a biological sample using target-analyte capture bodies that settle into predetermined locations within a transparent tube and labeling of the captured analyte. (See col. 1, lines 8-17). Levine '674 discloses a method and device for separating blood into components using a tube with a float that has a bore and removing the target sample with a needle. As neither Levine '362 nor Levine '674 teaches the density and size of a particulate carrier, the references fail to include all of the claim limitations. The presently claimed invention is nonobvious over the Levine references. Withdrawal and reconsideration of the rejection is respectfully requested.

Rejection of Claims 1, 5-13, and 14-18 under 35 U.S.C. § 103(a) as being unpatentable over Levine et al. (US Patent 5,635,362) in view of Van Vlasselaer (US Patent 5,474,687)

The Examiner has rejected claims 1, 5-13, and 14-18 under 35 U.S.C. § 103(a) as being unpatentable over US Patent 5,635,362 to Levine et al. (Levine '363) in view of US Patent 5,474,687 to Van Vlasselaer (Van Vlasselaer '687). The Examiner states that it would have been to one obvious skilled in the art to substitute the density beads of Levine '362 with those of Van Vlasselaer '687. Applicants respectfully traverse this rejection.

As stated above, Levine '362 teaches a one-step method for determining the presence or absence of a target analyte in a biological sample using target analyte capture bodies that settle into predetermined locations within a transparent tube and labeling of the captured analyte. (See col. 1, lines 8-17.) Van Vlasselaer '687 teaches a method for high yield enrichment of progenitor cells

based on density gradient centrifugation. (See col. 5, lines 13-15). More specifically, the method utilizes a precisely determined density solution (1.0605 ± 0.0005 g/ml) of a density gradient solution contained within a specially designed cell-trap centrifuge tube to allow the CD 34^+ cells to be collected by decantation. (See col. 5, lines 15-19 and 42-45). The efficiency of the method is improved when it is combined with the use of cell type specific binding agents such as antibodies conjugated to heavy carrier particles in a manner by which the antibodies bind to antigens expressed by undesired cell populations, causing them to have a higher density so that they are pelleted during centrifugation. (See col.3, lines 16-22).

The present invention discloses and claims a method for separating targeted components using a container that has a focusing device with a passage for receiving and elongating layers of the sample that are forced into the passage. As explained in the Specification, page 4, line 25 to page 5, line 7, the target component of the present invention collects in the through passage of focusing device. Neither Levine '362 nor Van Vlasselaer '687 discloses a bore or other passage for receiving and elongating the layers of the sample. Further, Van Vlasselaer '687 teaches that the beads are those that are heavier than CD 34^+ cells (col. 3, lines 16-23; col. 11, line 65-68), and that a specifically designed tube must be used (col. 5, lines 15-19). On skilled in the art would not have been motivated to substitute the beads of Van Vlasselaer '687 with those of the present invention because: i) it is the solution, not the beads, that are significant to the method of Van Vlasselaer '687; ii) the method requires a special centrifuge tube so that the unwanted components can be poured off (col. 7, lines 26-28); and iii) the density of the beads must be greater than 1.08 g/ml (col. 11, lines 56-59). As such, there is no likelihood of success of the combination because the invention of Van Vlasselaer '687 is very specific. Further, the references, alone or in combination, fail to teach all of

the limitations of the claimed invention. The present invention is nonobvious over Levine '362 and Van Vlasselaer '687. Withdrawal and reconsideration of the rejection is respectfully requested.

Rejection of Claims 19-22, and 24-30 under 35 U.S.C. § 103(a) as being unpatentable over Levine et at. (US Patent 5,393,674) in view of Van Vlasselaer (US Patent 5,474,687).

The Examiner has rejected claims 19-22, and 24-30 under 35 U.S.C. § 103(a) as being unpatentable over US Patent 5,393,674 to Levine et al. (Levine '674) in view of US Patent 5,474,687 to Van Vlasselaer (Van Vlasselaer '687). The Examiner states:

> It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include a particulate carrier that contains antibody having a binding affinity for a specific sample constituent and having a density of about 1.0 to 1.06g/cc and a size of about 4 to 5 microns as taught by Van Vlasselaer in the method of Levine et al. (US 5,393,674). One of ordinary skill in the art would have been motivated to include a particulate carrier that contains antibody having a binding affinity for a specific sample constituent and having a density of about 1.0 to 1.06g/cc and a size of about 4 to 5 microns in the method of Levine et al. (US Patent 5,393,674) for the advantage of providing for a rapid and high yield procedures to enrich for cell of interest and processing a complete sample would not requires no specialized instrumentation (Van Vlasselaer: col. 3, lines 22-28 and 43-45). Since both Levine et al. (US Patent 5,393,674) and Van Vlasselaer disclose the method of blood cell separation by centrifugation (Levine et al. (US Patent 5,393,674): col. 1, lines 7-14; fig. 1 and fig. 4; Van Vlasselaer: col. 2, lines 59-63).

Applicants respectfully traverse this objection.

The present invention teaches a method of harvesting a component from a sample, which entails mixing the sample with a particulate carrier that has a density of 1.0 to 1.06 g/cc and a size of 4 to 5 microns along with an antibody that has an affinity for the target. Levine '674 does not teach the use of carrier particles for harvesting of the targeted components. Van Vlasselaer '687 teaches the use of commercially available carrier particles having densities greater than 1.08 g/ml (col. 11, lines 65 to col. 12, lines 1-3; claim 7) along with a gradient solution that has a density gradient solution that has a density of 1.0605 ± 0.0005 g/ml (col. col. 5, lines 42-45). Van Vlasselaer '687

fails to teach a density for the beads of 1.0 to 1.06 g/cc. Further, Van Vlasselaer '687 specifically says that the method is to be practiced with a special centrifuge tube. One skilled in the art would not have been motivated to combine Levine '674 and Van Vlasselaer '687 to arrive at the present claimed invention because of the differences in the tubes. Finally, the references, alone or in combination fail to teach of all of the limitations of the claimed invention. Withdrawal and reconsideration of the rejection is respectfully requested.

Rejection of claims 31, and 33-36 under 35 U.S.C. § 103(a) over Levine et al. (US Patent 5,393,674) in view of Van Vlasselaer (US Patent 5,474,687)

The Examiner has rejected claims 31, and 33-36 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,393,674 to Levine et al. (Levine '674) in view of U.S. Patent 5,474,687 to Van Vlasselaer (Van Vlasselaer '687). The Examiner states:

> It would have been obvious to one of ordinary skill in the art at the time the invention was made to include particulate carrier that contains antibody having a binding affinity for a specific sample constituent and having a density of about 1.0 to 1.06 g/cc as taught by Van Vlasselaer in the method of Levine et al. (US 5,393,674)., One of ordinary skill in the art would have been motivated to include a particulate carrier that contains antibody having a binding affinity for a specific sample constituent and having a density of about 1.0 to 1.06 g/cc and a size of about 4 to 5 microns in the method of Levine et al. (US 5393674) for the advantage of providing for a rapid and high yield procedures to enrich for cell of interest and processing a complete sample would requires no specialized instrumentation (Van Vlasselaer: col. 3. lines 22-28 and 43-45). Since both Levine et at. US5393674 and Vlasselaer disclose the method of blood cell separation by centrifugation (Levine et al."674: col. 1, lines 7-14, fig. 1 and fig. 4; Van Vlasselaer: col. 2. lines 59-63).

Applicants respectfully traverse this rejection.

Claim 31 recites a method of harvesting targeted components from a whole blood sample using a first and second carrier particle, the first carrier particle directed to the target component, the second carrier particle to white blood cells.

As discussed above, Levine '674 fails to teach a particulate carrier that contains an antibody having a binding affinity for a specific sample constituent having a density of about 1.0 to 1.06 g/cc. As discussed above, Van Vlasselaer '687 teaches carrier particles of density greater than the gradient solution. Neither reference, either alone or in combination, teaches or suggests the recited combination of carrier particles with defined functional limitations as in claim 31. As the references do not contain every element of present claims, the references fail to provide a *prima facia* case of obviousness over the claimed invention. Withdrawal and reconsideration of the rejection is respectfully requested.

CONCLUSION

All amendments to the claims are made to advance prosecution. Applicants believe that the claims are in condition for allowance and request a notice of allowance be issued at the earliest convenience of the Examiner.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Jaconda Wagner (Reg. No. 42,207) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-1666 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

Jaconda Wagner
Attorney for the Applicant(s)
Registration No. 42,207

Becton Dickinson and Company
1 Becton Drive
Franklin Lakes, New Jersey 07417
(201) 847-6659

67451v3